

CLAIMS

What is claimed is:

1. An isolated nucleic acid fragment encoding all or a substantial portion of a cyclin A protein comprising a member selected from the group consisting of:

5 (a) an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:2, 4 and 6;

10 (b) an isolated nucleic acid fragment that is substantially similar to an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:2, 4 and 6; and

15 (c) an isolated nucleic acid fragment that is complementary to (a) or (b).

2. The isolated nucleic acid fragment of Claim 1 wherein the nucleotide sequence of the fragment comprises all or a portion of the sequence set forth in a member selected from the group consisting of SEQ ID NO:1, 3 and 5.

3. A chimeric gene comprising the nucleic acid fragment of Claim 1 operably linked to suitable regulatory sequences.

4. A transformed host cell comprising the chimeric gene of Claim 3.

5. A cyclin A polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:2, 4 and 6.

20 6. An isolated nucleic acid fragment encoding all or a substantial portion of a cyclin delta-1 comprising a member selected from the group consisting of:

25 (a) an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:8, 10, 12, 14 and 16;

(b) an isolated nucleic acid fragment that is substantially similar to an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:8, 10, 12, 14 and 16; and

30 (c) an isolated nucleic acid fragment that is complementary to (a) or (b).

7. The isolated nucleic acid fragment of Claim 6 wherein the nucleotide sequence of the fragment comprises all or a portion of the sequence set forth in a member selected from the group consisting of SEQ ID NO:7, 9, 11, 13 and 15.

35 8. A chimeric gene comprising the nucleic acid fragment of Claim 6 operably linked to suitable regulatory sequences.

9. A transformed host cell comprising the chimeric gene of Claim 8.

10. A cyclin delta-1 polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:8, 10, 12, 14 and 16.

5 11. An isolated nucleic acid fragment encoding all or a substantial portion of a cyclin delta-2 protein comprising a member selected from the group consisting of:

- (a) an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:18, 20 and 22;
- (b) an isolated nucleic acid fragment that is substantially similar to an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:18, 20 and 22; and
- (c) an isolated nucleic acid fragment that is complementary to (a) or (b).

12. The isolated nucleic acid fragment of Claim 11 wherein the nucleotide

15 sequence of the fragment comprises all or a portion of the sequence set forth in a member selected from the group consisting of SEQ ID NO:17, 19 and 21.

13. A chimeric gene comprising the nucleic acid fragment of Claim 11 operably linked to suitable regulatory sequences.

14. A transformed host cell comprising the chimeric gene of Claim 13.

20 15. A cyclin delta-2 polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:18, 20 and 22.

16. An isolated nucleic acid fragment encoding all or a substantial portion of a cyclin delta-3 comprising a member selected from the group consisting of:

- (a) an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:24, 26 and 28;
- (b) an isolated nucleic acid fragment that is substantially similar to an isolated nucleic acid fragment encoding all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:24, 26 and 28; and
- (c) an isolated nucleic acid fragment that is complementary to (a) or (b).

25 17. The isolated nucleic acid fragment of Claim 16 wherein the nucleotide sequence of the fragment comprises all or a portion of the sequence set forth in a member selected from the group consisting of SEQ ID NO:23, 25, and 27.

30 18. A chimeric gene comprising the nucleic acid fragment of Claim 16 operably linked to suitable regulatory sequences.

35 19. A transformed host cell comprising the chimeric gene of Claim 18.

20. A cyclin delta-3 polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:24, 26 and 28.

5 21. A method of altering the level of expression of a cyclin protein in a host cell comprising:

- (a) transforming a host cell with the chimeric gene of any of Claims 3, 8, 13 and 18; and
- (b) growing the transformed host cell produced in step (a) under conditions that are suitable for expression of the chimeric gene

10 wherein expression of the chimeric gene results in production of altered levels of a cyclin protein in the transformed host cell.

22. A method of obtaining a nucleic acid fragment encoding all or a substantial portion of the amino acid sequence encoding a cyclin protein comprising:

- (a) ~~probing a cDNA or genomic library with the nucleic acid fragment of any of Claims 1, 6, 11 and 16;~~
- (b) identifying a DNA clone that hybridizes with the nucleic acid fragment of any of Claims 1, 6, 11 and 16;
- (c) isolating the DNA clone identified in step (b); and
- (d) sequencing the cDNA or genomic fragment that comprises the clone isolated in step (c)

20 wherein the sequenced nucleic acid fragment encodes all or a substantial portion of the amino acid sequence encoding a cyclin protein.

25 23. A method of obtaining a nucleic acid fragment encoding a substantial portion of an amino acid sequence encoding a cyclin protein comprising:

- (a) synthesizing an oligonucleotide primer corresponding to a portion of the sequence set forth in any of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25 and 27; and
- (b) amplifying a cDNA insert present in a cloning vector using the oligonucleotide primer of step (a) and a primer representing sequences of the cloning vector

30 wherein the amplified nucleic acid fragment encodes a substantial portion of an amino acid sequence encoding a cyclin protein.

24. The product of the method of Claim 22.

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35 26. A method for evaluating at least one compound for its ability to inhibit the activity of a cyclin protein, the method comprising the steps of:

- (a) transforming a host cell with a chimeric gene comprising a nucleic acid fragment encoding a cyclin protein, operably linked to suitable regulatory sequences;

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(b) growing the transformed host cell under conditions that are suitable for expression of the chimeric gene wherein expression of the chimeric gene results in production of the cyclin protein encoded by the operably linked nucleic acid fragment in the transformed host cell;

(c) optionally purifying the cyclin protein expressed by the transformed host cell;

(d) treating the cyclin protein with a compound to be tested; and

(e) comparing the activity of the cyclin protein that has been treated with a test compound to the activity of an untreated cyclin protein,

10 thereby selecting compounds with potential for inhibitory activity.

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